K043011/A1

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April 4, 2005

Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Office of Device Evaluation
Food and Drug Administration
9200 Corporate Blvd.
Rockville, Maryland 20850 USA

RE: **K043011 Request for Evaluation of Automatic Class III Designation Under 513(f)(2)**

Submitted by: **Tm Bioscience Corporation**
Establishment Number 3002777243

Dear FDA:

510(k) Number for NSE Finding:

Tm Bioscience Corporation respectfully requests that premarket notification number *K043011* be considered for a risk-based classification of the *Tag-It™ Cystic Fibrosis Kit (cystic fibrosis mutation detection kit).* A "not substantially equivalent" decision was rendered for 510(k) # K043011 on April 1, 2005.

Statement of Cross Reference to 510(k):

Tm Bioscience Corporation hereby cross-references information contained in 510(k) #K043011.

Classification Being Recommended:

Tm Bioscience Corporation believes the documentation presented in premarket notification K043011 is sufficient to substantiate an order classifying the Tag-It™ Cystic Fibrosis Kit as Class II (general and special controls) pursuant to section 513 of the Federal Food, Drug and Cosmetic Act.

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Benefit / Risk Assessment:

The benefits and risks to health associated with CFTR genotyping tests have been evaluated by several professional bodies including the National Institute of Health (NIH), American College of Medical Genetics (ACMG), American College of Obstetricians and Gynecologists (ACOG), Center for Disease Control (CDC), and the Cystic Fibrosis Foundation (CFF). These evaluations have resulted in published recommendations for genetic testing in several populations, including those for which the Tag-It™ Cystic Fibrosis Kit is indicated.

There are no known direct risks to patient health associated with the Tag-It™ Cystic Fibrosis Kit. However, failure of the test to perform as indicated or error in interpretation of results may lead to improper clinical recommendations and/or patient management. When used in carrier screening in adults, a false-negative or false-positive interpretation could lead to inaccurate estimates of a couple's risk of having a child with cystic fibrosis. When used as an aid in newborn screening and/or confirmatory diagnosis of CF, a false-negative result could lead to a delay in definitive diagnosis and treatment; a false-positive result could lead to diagnostic analysis and genetic counseling which would otherwise be unnecessary.

Clinical variability of the disease based on the genotype-phenotype correlation variation for different mutations may result in the need for genetic counseling. Genetic counseling will enable individuals and couples to receive accurate information about risks and prognostic factors, allowing fully informed decision-making.

When used in CF carrier detection, the Tag-It™ Cystic Fibrosis Kit may identify: (i) positive/positive, positive/negative, and negative/negative couples; (ii) individuals who have a family history of CF; (iii) otherwise healthy males who carry mutations or variants associated with infertility. Interpretation of results will depend on the patient demographics, and must take into consideration that some mutations are more common in certain populations.

Since the Tag-It™ Cystic Fibrosis Kit, detects a limited number of mutations (out of more than 1300 mutations identified in the CFTR gene), it should not be used alone to diagnose cystic fibrosis. Assay results should be interpreted only in the context of the overall testing algorithm and clinical status of the patient.

Proposed General and Special Controls:

Tm Bioscience Corporation believes that general controls and special controls in accordance with the FDA draft Class II Special Control Guidance Document for CFTR Genotyping Tests constitute adequate information to ensure reasonable assurance of the safety and effectiveness of the Tag-It™ Cystic Fibrosis Kit assessed in K043011 via the premarket notification process 21 CFR 807. These controls parallel the safety and

effectiveness information provided in K043011 for the intended use, as stated in the submission:

Intended Use

The Tag-It™ Cystic Fibrosis Kit is a device used to simultaneously detect and identify a panel of mutations and variants, including those currently recommended by the American College of Medical Genetics / American College of Obstetricians and Gynecologists (ACMG/ACOG), in the cystic fibrosis transmembrane conductance regulator (CFTR) gene in human blood specimens. The Tag-It™ Cystic Fibrosis Kit is a qualitative genotyping test which provides information intended to be used for carrier testing in adults of reproductive age, as an aid in newborn screening, and in confirmatory diagnostic testing in newborns and children.

The kit is not indicated for use in fetal diagnostic or pre-implantation testing. This kit is also not indicated for stand-alone diagnostic purposes.

If there are any questions regarding this submission, please contact me by phone at 416-593-4323 ext. 335 or by fax at 416-593-2500.

Kind Regards,
Tm Bioscience Corporation

Alan Coley
Vice President
Operations